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## **Haemophilic knee arthropathy: long-term outcome after total knee replacement**

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**Abstract:** **PURPOSE:** The objective of this study was to evaluate the long-term outcome and prosthetic survival of primary total knee arthroplasty in haemophilic patients. It was hypothesized that the infection and revision rate are higher and the outcome inferior when compared with patients without haemophilia. **METHODS:** Between 1985 and 2004, forty-three consecutive primary total knee replacements were performed in thirty haemophilic patients. These patients' charts were reviewed retrospectively. Twenty-five patients (34 knees) were available for clinical and radiological follow-up. The outcome was assessed using the Knee Society score, WOMAC and Kaplan-Meier survivorship analysis. **RESULTS:** An haematogenous infection occurred in two patients. In three patients, component revision was needed: two because of an infection and one because of a mechanical failure. After a mean follow-up of 9.6 years (2-20), 94% of the patients rated their result as either excellent or good. At time of follow-up, the Knee Society Score averaged 73.3 points (range, 29-100) and showed a significant gain ( $p < 0.001$ ) compared to preoperative. Flexion contracture could be reduced significantly ( $p < 0.001$ ) from 18.1° preoperatively to 8.4° at follow-up, whereas flexion remained unchanged. When infection or any component replacement was set as endpoints, the 10 years prosthetic survival was 90 and 86%, respectively. **CONCLUSION:** Total knee arthroplasty in haemophilic patients is a reliable treatment that results in pain relief and functional improvement with a low risk of postoperative infection. However, neither the postoperative infection rate nor the functional result does reach the same level as in a population not affected by haemophilia.

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# Haemophilic knee arthropathy: long-term outcome after total knee replacement

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## Abstract

**Purpose** The objective of this study was to evaluate the long-term outcome and prosthetic survival of primary total knee arthroplasty in haemophilic patients. It was hypothesized that the infection and revision rate are higher and the outcome inferior when compared with patients without haemophilia.

**Methods** Between 1985 and 2004, forty-three consecutive primary total knee replacements were performed in thirty haemophilic patients. These patients' charts were reviewed retrospectively. Twenty-five patients (34 knees) were available for clinical and radiological follow-up. The outcome was assessed using the Knee Society score, WOMAC and Kaplan–Meier survivorship analysis.

**Results** An haematogenous infection occurred in two patients. In three patients, component revision was needed: two because of an infection and one because of a mechanical failure. After a mean follow-up of 9.6 years (2–20), 94% of the patients rated their result as either excellent or good. At time of follow-up, the Knee Society Score averaged 73.3 points (range, 29–100) and showed a

significant gain ( $p < 0.001$ ) compared to preoperative. Flexion contracture could be reduced significantly ( $p < 0.001$ ) from  $18.1^\circ$  preoperatively to  $8.4^\circ$  at follow-up, whereas flexion remained unchanged. When infection or any component replacement was set as endpoints, the 10 years prosthetic survival was 90 and 86%, respectively. **Conclusion** Total knee arthroplasty in haemophilic patients is a reliable treatment that results in pain relief and functional improvement with a low risk of postoperative infection. However, neither the postoperative infection rate nor the functional result does reach the same level as in a population not affected by haemophilia.

**Level of evidence** IV.

**Keywords** Knee · Total knee arthroplasty · Haemophilia · Prosthetic survival

## Introduction

Literature on total knee arthroplasty (TKA) in advanced haemophilic knee arthropathy reports on varying results and impact [7, 13, 15, 19, 21–23]. Besides of the generally documented pain relief and functional improvement after TKA, it is also known that the need for coagulation factor concentrates is reduced postoperatively [3]. However, different reports have shown high rates of complications including bleeding, deep infections and prosthetic failures [15, 19, 21, 23]. Many series contain small numbers of patients, or the follow-up period is short [3, 12, 13, 22]. There is only one study [7] demonstrating good results in a larger collective with a long follow-up period.

The purpose of the present study was to evaluate the subjective and objective outcome from a single centre (with different orthopaedic surgeons) with a considerable

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number of patients and a long follow-up period after primary TKA in a haemophilic population and to evaluate the rate and cause of failures. We hypothesized that the infection and revision rate are higher and the long-term outcome inferior than in the literature reporting on TKA in patients without haemophilia.

## Materials and methods

In a retrospective review, a consecutive, non-selective series of haemophilic patients who underwent primary total knee replacement at our institution was analysed. The minimum follow-up time was 2 years. The study was approved by the responsible investigational review board, and all patients gave their written informed consent.

From 1985 to 2004, forty-three primary total knee replacements were performed in thirty haemophilic patients. The average age at time of surgery was 44 (range, 23–68 years). Twenty-six patients had a factor-VIII deficiency (20 severe, five moderate and one mild) and four (one severe and three moderate) had a factor-IX deficiency [25].

In addition, 4 patients (13%) were HIV positive and their preoperative CD4 count averaged 406 cells/mm<sup>3</sup> (range, 136–730 cells/mm<sup>3</sup>). Only one patient had a low titer inhibitors against clotting factor.

According to the classification of Alberg et al. [2] and Petersson et al. [17], the average grade of osteoarthritis present was 4 (range, 3–5) and 8 (range, 4–10), respectively.

Surgery was performed bilaterally in 13 patients (43%). Seven different implants were used: (21) Duracon (Stryker, Kalamazoo, MI, USA), (10) porous-coated anatomic (PCA) total knee replacement (Howmedica, Rutherford, NJ, USA), (5) self aligning (SAL) knee prosthesis (Sulzer Medica, Winterthur, Switzerland), (3) Innex (Sulzer Medica, Winterthur, Switzerland), (2) Wallaby II (Sulzer Medica, Winterthur, Switzerland), (1) Natural Knee (Zimmer, Warsaw, IN, USA) and (1) Rotating hinge RT-Solution Endoplus (Plus Orthopaedics, Rothkreut, Switzerland).

All patients were treated with their specific factor-VIII or factor-IX product, they used for home-self-treatment, in either prophylactic or majority on demand factor replacement. Approximately two-third used plasmatic factor, and the others used different recombinant factors. The treating haematologists accompanied all surgeries from start of anaesthesia until the end period of the procedure to ensure sufficient factor replacement. For starting and during surgery, factor level of 100% was aimed (reached by 50 IE FVIII/per kg body weight, respectively, 80–100 IE FIX/kg BW), usually by one dose before and the second dose after opening of tourniquet calculated by the blood loss. The first 2 days either continuous infusion or injections every 4–6 h were given aiming at factor levels between 70 and 100%.

From day 3, the dose was tapered to through levels between 50 and 70% up to day 6, then for another 3 days to through levels between 40 and 60%. In our observation, day 9 seemed to be critical because of dropping off eschar from the wounds; therefore, further dose reduction started only at day 10. During the physiotherapy period, they had a full prophylaxis to keep through level above 5–10%. All haemophiliacs with severe or moderate did not receive medical thrombosis prophylaxis.

Out of the thirty patients, four (five knees) had died due to causes unrelated to surgery at a mean of 3.6 years (range, 0.6–7.3) after the index procedure. One patient who had emigrated could not be traced. The available clinical and radiological data on these five patients were used for the analysis. The remaining twenty-five patients (thirty-seven knees) were available to complete follow-up examinations. For those patients that had revision surgery, time of the revision surgery was defined as follow-up endpoint. Table 1 summarizes the population and provides details on the evaluation.

## Clinical assessment

Preoperatively as well as at the time of follow-up, the clinical assessment included a structured interview and a detailed, standardized physical examination. At the time of follow-up, the Knee Society Clinical Rating System (KSS) [9] and Western Ontario and McMaster OA Index (WOMAC) [4] were recorded. The WOMAC consist of 24 items addressing the three dimensions: pain, stiffness and physical function. Items were scored with a rating system consisting of 5 grades (no = 0, mild = 2.5, moderate = 5, severe = 7.5, extreme = 10 points). The dimension scores were calculated as the mean of the items, with 10 representing worst pain, stiffness and physical function.

**Table 1** Patient population

	No of knees	No of patients	Follow-up	Evaluation
Total (1985–2004)	43	30	8.6 years (0.5–19.0)	Protheses survivorship preoperative knee society score chart review
Lost to follow-up (death)	6	5		
Revised before follow-up	3	3		Post-knee society score before revision
Available for follow-up	34	25	9.6 years (2–20)	Post-knee society score WOMAC

Additionally, patients were asked to rate the result as excellent, good, fair or poor. The follow-up interview and clinical examination were completed by surgeons different from the operating surgeons.

The patients' charts were reviewed for preoperative comorbidities, to determine the preoperative KSS score, to note remarkable intraoperative events and record postoperative complications (postoperative bleeding, infection, revision surgery). Haematological charts were reviewed for the patients HIV status, the CD 4 account and inhibitors against clotting factor.

#### Radiological assessment

Preoperatively and at the time of follow-up, standard radiographs (AP view, lateral view, patella sunrise view and long-leg standing radiographs) were taken. However, the preoperative conventional and long-leg standing radiographs were available only in 39 and 21 patients, respectively. The pre- and postoperative radiographs were judged with regard to evaluation of the mechanical axis of the leg and signs of loosening of the prosthesis.

#### Statistical analysis

Statistical analyses were performed by a statistical consultant. The paired Wilcoxon signed-rank test was used to compare the values at the time of diagnosis with those at the time of follow-up. The Spearman rank correlation was applied to correlate different variables. The Mann–Whitney test was used for unpaired groups. Five and 10 years rates of survival of the prostheses and their confidence intervals

were calculated with use of a Kaplan–Meier survival curve. The endpoint for survivorship analysis was revision in terms of either any components replacements and conversion to an arthrodesis or an infection.

All statistical analyses were performed using SPSS 13.0 for MacIntosh OS X. The significance level was set at  $p < 0.05$ .

## Results

Table 2 summarizes early and late postoperative complications. No clinical manifestation of thrombosis or pulmonary embolism was observed.

Of the 43 total knee replacements, three were complicated by an infection. Two were acute haematogenous infections. Both were managed by surgical irrigation and debridement and with an additional polyethylene inlay exchange in one of them. A third infection was caused by a direct trauma with knee perforation and rupture of the patellar ligament. A conversion to an arthrodesis was performed. This patient was not included for calculation of infection-free prosthetic survivalship.

Out of the 43 knees, three required component removal. One patient had revision surgery because aseptic loosening of the tibial component 9 years postoperatively. No specific reason for this early failure was found. The two other patients, as mentioned earlier, had a replacement of the polyethylene and a conversion to an arthrodesis, respectively.

Table 3 summarizes the Knee Society Score, the WOMAC and the subjective overall result at latest follow-up. Both,

**Table 2** Postoperative complications

	Number	Postoperative complications	
		Details	Management
Postoperative haemarthrosis	11		1 joint aspiration 3 surgical evacuation
Arthrofibrosis	3	All had postoperative haemarthrosis	Surgical arthrolysis at 3, 12 and 14 months
Infection	3	pt 1: acute haematogenous; HIV positive; 2 pneumococcus sepsis after 7 + 9 years	Irrigation + arthroscopic debridement after 7 years; permanent antibiotic suppression after 9 years
		pt 2: acute haematogenous; Staphylococcus aureus	Irrigation debridement polyethylene inlay exchange after 8 years
		pt 3: direct trauma with open wound + rupture of patellar ligament; secondary deep infection; non-complaint drug abuser	Arthrodesis after 2 years
Component removal	3	pt 1: aseptic loosening tibial component	Revision surgery with component removal after 9 years
		pt 2: acute haematogenous; Staphylococcus aureus	Irrigation, debridement + polyethylene inlay exchange after 8 years
		pt 3: secondary infection after direct trauma	Arthrodesis after 2 years
Additional surgery	1	Persisting femoropatellar pain + recurrent effusion	Patella component implantation after 1 year

**Table 3** Pre- and postoperative Knee Society Score, WOMAC and subjective overall result

	Preoperative			Postoperative			p-value
	Mean	Range	SD	Mean	Range	SD	
Follow-up (years)				9.4	2–20		
Age at follow-up (years)				53	36–80		
<i>Knee society clinical score</i>							
Pain (max., 50 points)	15	0–45	10	43	10–150	12	<0.001
Range of motion (max., 25 points)	14	0–26	6	16	4–25	6	
Flexion	89	25–130	26	89	40–150	25	
Flexion contracture	18	0–45	12	8	0–30	10	<0.001
Stability (max., 25 points)	24	15–25	3	24	15–25	3	
Deductions (max., 50 points)	16	0–36	10	8	0–30	8	<0.001
Total score	36	15–90	16	73	29–100	18	<0.001
<i>Knee society functional score</i>							
Walking (max., 50 points)	30	10–40	10	43	20–25	7	<0.001
Stairs (max., 50 points)	34	15–50	10	40	15–50	11	0.005
Deductions (max., 20 points)	2	0–10	4	0	0–10	2	0.003
Total score	62	15–90	19	83	40–100	15	<0.001
<i>WOMAC</i>							
Pain				0.8	0–5	1.3	
Stiffness				1.6	0–10	2.8	
Function				1.9	0–6	1.9	
Total				1.4	0–7	1.8	
<i>Subjective overall result</i>							
				26	Excellent		
				8	Good		
				1	Fair		
				1	Poor		

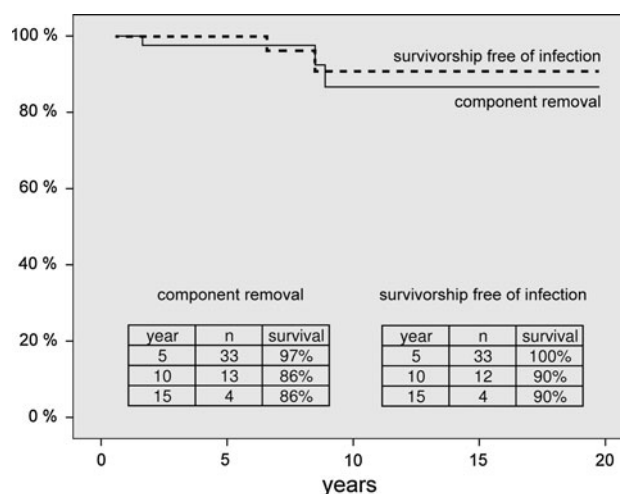
the mean Knee Society clinical and functional Scores had increased significantly ( $p < 0.001$ ) from pre- to postoperative. Postoperative measurements of active motion demonstrated that the mean average flexion contracture had significantly decreased by  $10^\circ$  ( $p < 0.001$ ), but was not normalized. No significant improvement was seen in maximal knee flexion attained.

Standardized conventional radiographs and long-standing X-rays made at the time of follow-up were available for all 37 knees. Radiographic results revealed signs of osteolysis or loosening of components in four patients.

Figure 1 illustrates implant survivorship with respect to component removal and survivorship free of infection at any point.

## Discussion

The most important findings of the present study were that surgery resulted in high patient's satisfaction and in a significant improvement of knee function. However, postoperative knee flexion showed no improvement, and the preoperative flexion contracture was significantly reduced



**Fig. 1** Survivorship with respect to component removal for any reason and free of infection at any point

but not normalized. As it was hypothesized, the infection and revision rate were higher and the clinical outcome inferior than in the literature reporting on TKA in patients without haemophilia.

In this series, the infection rate was 5%. This is clearly higher compared with the prevalence of infection of under 2% [10, 16, 18] in a non-haemophilic population and still slightly increased, but consistent with the two most recently reported series [7, 22] in haemophilics that have shown a prevalence of 1.4 and 3%, respectively. However, the infection rates in the literature in general for total knee arthroplasty in haemophilic patients are ranging from 0 to 17% [13, 15, 23]. No concise and specific explanation can be given for the relatively low infection rate in our series.

There is a continuing controversy in the literature whether HIV infection increases the risk of infection. Ragni et al. [19] reported a rate of 26% in HIV-positive patients with haemophilia with CD4 counts < 200 cells/mm<sup>3</sup>. In accordance, Hicks et al. [8] demonstrated higher rates of postoperative infection in patients' sero-positive for HIV. However, others [8, 15] could not find evidence that a positive HIV status had any negative effects on the infection rate. Therefore, it remains unknown if the relatively small percentage of HIV-positive patients (9%) was related to the low prevalence of infection in our collective. Similarly, none of the two series [7, 22] with low infection rate could provide an answer why infection had not been a common problem in their collective. Most probably several factors are responsible for successful reduction of the infection rate, that is, adequate retroviral therapy at any time, sufficient factor replacement perioperatively, appropriate antisepsis during self-administration of factor concentrates and prophylactic antibiotics before invasive procedures with the potential risk for haematogenous spread of bacteria. In contrast to many other treatment centres, we never used medical thrombosis prophylaxis. This might have contributed to very low wound haemorrhage in the postoperative period.

The knee society score in this population did not reach the same level when compared with literature reporting on results after TKA in non-haemophilic patients [1, 5, 20]. However, relevant pain relief after the procedure was seen. In contrast, there was only a slight gain in ROM and only the flexion contracture could be reduced successfully. Nevertheless, patient's satisfaction and the knee society functional score were very high. The relatively fair range of motion achieved postoperatively was despite a standardized and intensive physiotherapeutic rehabilitation protocol known to play an important role [14] towards a successful TKA in haemophilic patients.

The postoperative WOMAC confirmed that patients in general had no or only mild pain, stiffness and considerably good function in activities of daily living. This marked discrepancy between subjective and objective results may be explained by the fact that these patients had learned to deal with increasing disability since their childhood and in consequence less demanding with regard to sports

activities and/or are suffering from limitations due to additional joint involvement.

With revision for any reason, we report of a five and 10 years prosthetic survival rate of 97 and 86%, respectively. These results are comparable to those observed by Goddard [7] (98% at 5 years; 87% at 10 years), Silva [23] (83% at 10 years), Rodrigues-Marchand [22] (97% at 7.5 years) and Norian [15] (90% at 5 years), but less favourable than in non-haemophilic patients with 90–97% at 10–15 years follow-up [1, 5, 11, 20].

There are some limitations for this study. First, this is a retrospective series with a limited number of patients what is inherent to the small prevalence of the pathology. However, we believe that the number is sufficient to allow valuable conclusion. Second, this study is lacking of a paired matched control group mainly because the difficulties to identify patients of the same time period matching for the typically young age and type of prosthesis. Nevertheless, the comparison of our data with literature on TKA in non-haemophilic patients can highlight important differences in the outcome.

With modern medical management, the life expectancy of haemophilic patients is nearing that of the general population, and the improvement in quality of life after total knee arthroplasty may outweigh the moderately higher risk of failure [13, 15]. However, with respect to this permanent disorder, it remains most important to start prophylactic treatment in early childhood [6, 24] to prevent recurrent intra-articular bleeding to reduce the risk of development of osteoarthritis. Therefore, continuous patients support and guidance from a haematologist should be established and particularly when total knee arthroplasty becomes necessary surgery should be performed in a comprehensive care centre allowing an interdisciplinary approach. And even if most recent studies report survivorships approaching those of non-haemophilics, patients should be informed about the still inferior survival of a total knee arthroplasty in haemophilics.

## Conclusion

Total knee arthroplasty in haemophilic patients is a reliable treatment that provides relevant benefits in terms of pain reduction and functional improvement. With a specialized multidisciplinary management, rates of postoperative complications and implant failures may be reduced. Nevertheless, when compared with a non-haemophilic population, less favourable infection and survival rates as well as functional results must be expected.

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